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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,296	09/13/2000	Patricia Anne Nuttall	2369-1-002	3816

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 04/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,296	NUTTALL ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,10,18,21-24,29-32 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,10,18,21-24,29-32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Upon reconsideration, the finality of the Office action mailed 03 May 2005 is hereby withdrawn in view of the new grounds of rejection set forth below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, 6, 10, 18, 21-24, 29-32, and 34 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to claim 32 at pg 4 of the previous Office Action (03 May 2005) is *withdrawn* in view of the amended claim (07 November 2005).

2. The rejection of claim 20 under 35 U.S.C. § 112, second paragraph as set forth at pg 10 of the previous Office Action (03 May 2005) is withdrawn in view of the cancelled claim (07 November 2005).

Claim Objections

3. Claim 1 is objected to because of the following informalities:

3a. Claim 1 recites "SEQ.ID.NO: 1". However, claim 1 should recite "SEQ ID NO: 1". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. Claims 1, 4, 6, 10, 18, 21-24, 29-32, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated histamine binding peptide capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M which comprises the amino acid sequence of SEQ ID NO: 4 and a method for treating

allergic asthma comprising administering the protein of SEQ ID NO: 4, *does not reasonably provide enablement for* (1) an isolated histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which has a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 or are positioned in a functionally equivalent complementarity of shape; (2) a method for treating or preventing allergic asthma comprising administering the proteins in part (1); or (3) a method of preventing allergic asthma comprising administering the D.RET6 protein of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. It is noted that this rejection was made in the Office Action of 10 June 2004 and was later withdrawn in the Office Action of 03 May 2005.

The claims also recite that a histamine or serotonin binding compound additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 131 in SEQ ID NO: 4. The claims recite that the compound is stabilized by either or both disulphide bridges formed between cysteines 179 and 151 of SEQ ID NO: 4. Claim 10 recites that the histamine or serotonin binding compound comprises a synthetic compound. The claims also recite that the compound is produced by recombinant DNA technology, is derived from blood-feeding ectoparasites, spiders, scorpions, or snakes and venomous animals, and is bound to a resin support.

The specification teaches that a functional equivalent means "compounds that possess the desired binding site and includes any macromolecule or molecular entity that binds to histamine or serotonin with a dissociation constant of 10^{-7}M or less and that possesses an equivalent complementarity of shape" (pg 6, lines 13-16). The specification also teaches that fragments is meant "any portion of the entire protein sequence that retains the ability to bind vasoactive amines with a dissociation constant of 10^{-7}M or less....Variants may include, for example, mutants containing amino acid substitutions, insertions or deletions from the wild type sequence of Figures 1 to 4" (pg 7, lines 12-18). However, the specification only teaches the binding *protein* comprising the amino acid sequence of SEQ ID NO: 4 and its characterization (pg 26-28). The specification does not teach any other histamine or serotonin binding proteins or functional equivalents complementary in shape. Furthermore, regarding functional equivalents of a protein, for example, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions.

Applicant's arguments set forth in the response of 13 December 2004, as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant argues that when determining the scope of protection, it is not proper to limit Applicant to the specific examples presented that illustrate a general phenomenon. Applicant points out that they should be allowed to cover all obvious modifications. Applicant asserts that the USPTO routinely grants claims that extend beyond the specific protein(s) that are disclosed in the specification so that the claims cover obvious equivalents of the specific protein(s). Applicant refers the Examiner to U.S. Patent 6,617,312 which formed the basis of a double patenting rejection and wherein the claims are not limited to a specific protein sequences but extend to homologous proteins with a sequence motif.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the current rejection is in compliance with the enablement requirement wherein the instant specification must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention (please see above and points ii-iv, below). Additionally, each Patent Application is examined on its own merits. The invention that was deemed allowable in one patent has no bearing on this application.

(ii) Applicant states that the specification teaches which residue positions of the D.RET6 protein (SEQ ID NO: 4) are important for the high affinity binding to serotonin and histamine and which amino acid residues may be located in these positions. Applicant argues that once the skilled person is equipped with this information, routine techniques may be employed to identify

other compounds having the properties set forth in the claims and cites pg 6-8 and 28 of the specification.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application discloses that about 70 amino acids of the D.RET6 sequence of SEQ ID NO: 4 should be conserved based upon sequence homology to other histamine binding proteins (see Figure 22, for example). The Examiner has also interpreted this disclosure as meaning that 139 amino acid positions out of the 209 total amino acids of SEQ ID NO: 4 (or 66% of the overall protein) are open to alterations. The claims are even broader yet, as they only require a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 or are positioned in a functionally equivalent complementarity of shape. However, the specification does not provide any guidance or working examples indicating which amino acid residues outside of the recited binding site are required for correct protein conformation and function. Relevant literature teaches that alterations in amino acid residues outside of binding/activation sites change protein conformation and/or dynamics. For example, Yoon et al. disclose that human IL-10 and Epstein-Barr virus homolog, vIL-10, share high sequence and structural similarity, but have functional differences (Structure 13: 551-564, 2005; pg 551). Yoon et al. determined the crystal structures of vIL-10/sIL-10R1 and hIL-10/sIL-10R1 and disclose that structural changes in the AB/CD loop region and the orientation of vIL-10 on the surface of IL-10R1 mediate vIL-10's affinity for IL-10R1 (pg 553, col 1). Yoon et al. also indicate that "amino acid substitutions in vIL-10 appear to disrupt the ability of the AB loop to adopt the proper geometry required for stable high

affinity sIL-10R1 binding" (pg 560, bottom of col 2). Additionally, Jeffery et al. determined the crystal structures of five mutant forms of *E.coli* aspartate aminotransferase and teach that the three-dimensional fold of each mutant enzyme is the same as that of the wild-type protein, but that there is a rotation of the mutated side chain around its Cα-Cβ bond, altering catalysis (Protein Engin 13(2): 105-112, 2000; abstract; bottom of pg 108 through pg 111, col 1). Jeffery et al. teach that "these results demonstrate how residues outside the active site can be important in helping determine the subtleties of the active site amino acid geometries and interactions and how mutations outside the active site can have effects on catalysis" (pg 105, abstract). Thus, undue experimentation would be required of the skilled artisan to generate the large number of derivatives of D.RET6 recited in the instant claims and screen the same for the desired activity. As discussed above and in the previous Office Action of 10 June 2004, certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in activity and in providing the correct three-dimensional spatial orientation of binding and active sites (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

(iii) Regarding the Examiner's citation of Wells and Ngo, Applicant contends that the field of computer-assisted or in silico analyses of amino acid sequences has advanced exponentially since these antiquated references were published. Applicant also asserts that critical residues implicated in vasoactive amine binding are identified and discussed throughout the specification. Applicant points to Figure 22, wherein an alignment of amino acid sequences of D.RET6 and related family members is presented and such critical residues are indicated. Applicant submits that D.RET6 and its structurally related family members are functionally related as well, in that

they all are capable of binding vasoactive amines. Applicant states that the specification provides the crystal structure of related family member, FS-HBP2, and that it would be a matter of routine practice to perform computer modeling to predict the crystal structures of the other related vasoactive amine binding protein family members (D.RET6) based on this solved crystal structure. Applicant indicates that guidance relating to sequence variation observed among the vasoactive amine binding family members and the implications of such variation is found at pg 34-35 of the specification. Applicant asserts that "structure + function" language has been adopted in the claims, such that only a protein that satisfies the sequence requirements of the claims and binds to histamine or serotonin with very high affinity is embraced. Applicant argues that the skilled practitioner would have no difficulty in identifying proteins that fall within the scope of the claims and thus no information is missing from the specification that would preclude such as skilled practitioner from practicing the invention across the entire scope. Applicant states that the references cited by the Examiner in the Action of 10 June 2004 have little bearing on the present invention and that the claimed invention is amply enabled by the specification and does not suffer the "pitfalls" described in the references.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in part (ii) above, the specification of the instant application discloses that about 70 amino acids of the D.RET6 sequence of SEQ ID NO: 4 should be conserved based upon sequence homology to other histamine binding proteins (see Figure 22, for example). The Examiner has also interpreted this disclosure as meaning that 139 amino acid positions out of the 209 total amino acids of SEQ ID NO: 4 (or 66% of the overall protein) are open to alterations. The claims are even broader yet, as they only require a binding site comprising amino acid

residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 or are positioned in a functionally equivalent complementarity of shape. However, the specification does not provide any guidance or working examples indicating which amino acid residues outside of the recited binding site are required for correct protein conformation and function. The broad brush discussion of making and screening for variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. The state of the art is such that polymorphs of an organic molecule cannot be predicted by computer modeling (Price, S., Adv Drug Delivery Rev 56: 301-319, 2004). Price teaches that there are many factors that make predicting crystal structures of organic materials a very different challenge from modeling traditional engineering materials, such as entropic factors, temperature, and the complexity of the energies of intramolecular and intermolecular interactions (pg 304, 311). Dahl et al. also disclose that "[w]hile it is quite straightforward to deduce the amino acid sequence of a protein from the DNA sequence of the gene encoding it, determining the three-dimensional molecular structure of proteins has proven to be more difficult...The average time it takes to solve an eukaryotic structure has been one to three years for soluble proteins" (Basic Clin Pharmacol Toxicology 96: 151-155, 2005; pg 152, 1st full ¶). Thus, it would not be a matter of routine practice to perform computer modeling to predict the crystal structures of the other related vasoactive amine binding protein family members based on the solved crystal structure of FS-HBP2.

According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of

experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis". The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such trial and error experimentation is considered undue. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

Additionally, Ngo et al. and Wells et al. were cited by the Examiner to emphasize that positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Ngo et al. state that decades of research have failed to produce an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone (pg 492, 2nd full paragraph). Wells et al. teach that "it is possible to modulate protein function by mutation at many contact sites" and "to design large changes in function will often require mutation of more than one functional residue" (pg 8509, first paragraph; emphasis added). Wells et al. disclose that more pronounced deviations

from simple additivity "can occur when the sites of mutations strongly interact with one another (by making direct contact or indirectly through electrostatic interactions or large structural perturbations) and/or when both sites function cooperatively" (pg 8515, column 2, 3rd full paragraph). For example, the stabilizing interaction between two side chains can be broken with one mutation and if the catalytic functions of two or more residues are interdependent, then a mutation of one residue can alter the functioning of the other(s) (pg 8512, column 2, 2nd full paragraph; pg 8515, column 1, 2nd full paragraph).

The other references were cited by the Examiner (Skolnick et al., Bork 2000, Doerks et al., Smith et al., Brenner et al., Bork 1996) to indicate that the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share

structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Thus, the skilled artisan would not be able to determine, without undue experimentation, the structural conformation and function of D.RET6 variants based upon linear amino acid sequences and one particular binding site. One skilled in the art would also not be able to determine, without undue experimentation, the positions in the D.RET6 protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Furthermore, undue experimentation would be required of the skilled artisan to treat or prevent allergic asthma by administering to a subject all histamine or serotonin binding proteins capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 or are positioned in a functionally equivalent complementarity of shape. A large quantity of experimentation would also be required of the skilled artisan to *prevent* allergic asthma by administering the histamine or

serotonin binding protein of SEQ ID NO: 4. There is little or no guidance in the instant specification or the post-filing date art to indicate that all histamine or serotonin binding proteins capable of binding to histamine or serotonin which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 will treat or prevent allergic asthma. There is also little or no guidance in the specification or post-filing date art to indicate that the protein of SEQ ID NO: 4 prevents allergic asthma. Undue experimentation would be required of the skilled artisan to determine the quantity of binding protein administered, the best route of administration, and the duration of treatment to treat/prevent allergic asthma.

Due to the large quantity of experimentation necessary to generate the infinite number of histamine or serotonin binding proteins recited in the claims, screen same for activity, and treat or prevent allergic asthma in a human or animal; the lack of direction/guidance presented in the specification regarding which structural features outside the binding site are required in order to provide proper structure/activity; the absence of working examples directed to same; the complex nature of the invention; and the state of the prior art which establishes that polymorphs of an organic molecule cannot be predicted by computer modeling; and the unpredictability of the effects of mutation on protein structure and function undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

5. Claims 1, 4, 6, 10, 18, 21-24, 29-32, and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is noted that this rejection was made in the Office Action of 10 June 2004 and was later withdrawn in the Office Action of 03 May 2005.

The specification teaches that a functional equivalent means "compounds that possess the desired binding site and includes any macromolecule or molecular entity that binds to histamine or serotonin with a dissociation constant of 10^{-7}M or less and that possesses an equivalent complementarity of shape" (pg 6, lines 13-16). However, the specification does not teach functional or structural characteristics of variants of SEQ ID NO: 4 or all possible histamine or serotonin binding proteins capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned substantially the same as residues 139, 71, 67, and 112 in SEQ ID NO: 4 in the context of a cell or organism. The description of one D.RET6 polypeptide species (SEQ ID NO: 4) is not adequate written description of an entire genus of functionally equivalent binding proteins which incorporate all variants and fragments capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV.

Applicant's arguments set forth in the response of 13 December 2004, as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant refers the Examiner to the arguments presented above and the amendments to the claims.

Applicant's arguments have been fully considered but are not found to be persuasive. The description of one D.RET6 polypeptide species (SEQ ID NO: 4) is not adequate written description of an entire genus of structurally and functionally equivalent binding proteins which incorporate all variants and fragments capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV. The specification of the instant application discloses that about 70 amino acids of the D.RET6 sequence of SEQ ID NO: 4 should be conserved based upon sequence homology to other histamine binding proteins (see Figure 22, for example). The Examiner has also interpreted this disclosure as meaning that 139 amino acid positions out of the 209 total amino acids of SEQ ID NO: 4 (or 66% of the overall protein) are open to alterations. The claims are even broader yet, as they only require a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4 or are positioned in a functionally equivalent complementarity of shape.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. However, in this case, the specification has not

shown a relationship between the structure and function of the claimed genus of variants of the protein of SEQ ID NO: 4. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The broad brush discussion of making or screening for variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
17 April 2006

ELIZABETH KEMMERER
PRIMARY EXAMINER